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From the United States Public Health Service and the Department of Physiology, Columbia University, New York

Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, in the Faculty of Pure Science

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Our object in undertaking this research was to acquire a more intimate knowledge of the specific effects of high environmental temperatures upon certain individual organs and tissues of the body, so that general effects as observed among furnace workers could be interpreted more accurately than has heretofore been possible.

Unfortunately, there are no animals in common use in the laboratory which are wholly suitable for such a study. Of the domestic animals the horse is perhaps to be preferred because of the greater similarity of its heat-controlling apparatus to that of man, but inasmuch as facilities for handling animals of this size were not available we were compelled to consider the smaller animals. Of these, dogs were selected as being the most tractable and, all things considered, the best adapted for the work which we planned to do. In making this selection it was frankly recognized that the dogs have developed a method of cooling the body by the evaporation of water which is strikingly different from that which obtains in the horse and man. However, in spite of this dissimilarity and its possible effects upon the gases of the blood, our results seem to indicate that any differences are quantitative and that the qualitative changes in gas content which result from exposure to high temperatures are the same for the two forms. Aside from this theoretical objection the dogs proved to be as nearly ideal as could be hoped for.

We have centered our attention on a single tissue—the blood. This tissue was chosen because of the rapidity and accuracy with which it reflects changes taking place throughout the organism, and because it is the only tissue which may be sampled at intervals and still leave the animal in what may be presumed to be an approximately normal condition. The blood was analyzed for oxygen content and capacity, carbon dioxide content and capacity, sugar and total solids,

[1] Approved for publication by the Surgeon General.

all of which were determined as a matter of routine. In a few cases the iron of the blood was determined as a control on the oxygen capacity. In a second series the hydrogen-ion concentration and the carbon dioxide content of the plasma were determined as routine, while an occasional determination of the lactic acid in the blood was made.

In presenting the data which we have accumulated, we are aware that various investigators, from the time of Claude Bernard on, have reported observations on the blood of animals which were exposed to high temperatures, but it seems to us that these results are not only fragmentary but in some cases of such doubtful accuracy that a clear-cut interpretation is practically impossible. The inaccuracies, where they exist, are due not only to faulty chemical technic but frequently to an abnormal condition of the animals. For example, many of them were subjected to anesthesia, which disturbs not only the heat-regulating mechanism but also the general metabolism of the subject. Furthermore, these observations were made at various times upon various species of animals, while in the present research we have endeavored to correlate as many data and data of as many different types as is practical on a given series of individuals of a single species.

In addition to the previously mentioned observations on the blood, we have recorded the rectal temperature and the body weight whenever a sample of blood was drawn, and in certain of the experiments even more frequently.

Methods: I. *Chemical.* *a. The blood gases.* The carbon dioxide content and capacity of the blood were determined by the methods of Van Slyke (1). The oxygen content and capacity were determined by the method of Van Slyke and Stadie (2), but we found it necessary to add three or four drops more of the potassium ferricyanide solution than is recommended by these authors, possibly because our ferricyanide was the product of a different manufacturer.

All of the results reported were obtained with the old form of the Van Slyke apparatus, having the short stem. This apparatus was checked against the newer form having the longer stem and the water jacket and we did not feel that the differences in the results were sufficient to warrant the extra time required by the latter apparatus; for this would have necessitated an additional observer and, in our opinion, the differences due to personal equation would have more than offset the greater precision of the later apparatus.

b. The sugar of the blood. MacLean's method for 1 cc. of blood (3), as modified by Hastings and Hopping (4), was used throughout the work.

c. The total *iron* of the blood was occasionally determined as a means of controlling the oxygen determinations, using the method published by Brown (5). In this work we found that the colorimeter gave a more satisfactory means of comparing the colors than did the method described by the author.

d. The *lactic acid* was determined by the method which we have described elsewhere (6) except that the filtrate was extracted with ether and the determination made on the ether extract instead of on the filtrate directly. This was done upon the suggestion of Dr. Isidor Greenwald, in order to avoid the disturbing influence of the sugar of the blood. It is recognized that this method is not specific for lactic acid but since we were unable to find indications of an increase we feel that it is sufficient to justify the conclusions which we have drawn.

f. The *total solids* were determined by drying 1 cc. of blood to constant weight in an electric oven at 110°C. This was done in duplicate in silica crucibles.

g. The hydrogen-ion concentration was determined by the colorimetric method described by Cullen (7). The phosphate solutions which were used as standards of comparison were checked by means of the potentiometer.

II. *Physical. a. The temperature chamber.* The chamber in which the animals were exposed to the various environmental conditions was constructed of two layers of beaver board separated by a 4-inch air space. The chamber contained three windows, one at one end, another on one side and a third on the top. These windows were each about 2 feet square, and consisted of two sheets of glass with a 2-inch air space between them. A gas stove was placed inside at one end, under the window; at the opposite end there was a single wooden door lined with beaver board. The inside dimensions of the chamber were 4 feet in width by 7 feet each in length and height.

The method of heating, of heat control and of ventilation was that described by Hastings (8), and it has proven very satisfactory. The gas flow was controlled by a Roux regulator. A 6-inch electric fan was installed to overcome stratification and pockets in addition to the use of convection currents as recommended by Hastings. Thermometers placed in various parts of the chamber showed no stratification or variations in temperature greater than one-half of one degree Centigrade, while the temperature of the chamber as a whole did not vary more than one degree throughout the day.

b. The *relative humidity* within the chamber was determined by means of a sling psychrometer.

c. The *body temperature* was taken by an ordinary certified 1-minute clinical thermometer inserted in the rectum. The thermometer was left in place for at least $1\frac{1}{4}$ minutes.

d. The *respiratory rate* was counted by means of a Fitz pneumograph writing on a smoked drum through a Marey tambour. This technic was made necessary by the extremely high rates of respiration encountered at the higher temperatures.

III. *Biological.* All of the dogs used in these experiments were adult, short-haired mongrels, varying in weight from 10 to 15 kilograms. They were kept, when not actually in use for the experiments, in a kennel on the roof, and were maintained in a healthy condition throughout. It is needless to say that they were used exclusively for the purpose of the research here reported.

Their diet consisted of bread and cooked meat in an amount at least sufficient to maintain their weight. As a matter of fact, most of them gained in weight during the course of the experiments. They received no food during the period of 18 hours preceding each experiment. No food or water was permitted during the period of the experiments.

It was our practice to bring the dog which was to be used for an experiment to the laboratory at least half an hour before actually beginning the work, in order that he might become quiet and somewhat accustomed to conditions and to the personnel of the laboratory before the initial sample of blood was drawn. A rest period of at least two weeks was permitted each dog between experiments to allow recovery from any deleterious effects caused by the high temperature or from the hemorrhage attendant upon the experiment.

During the exposure in the heat chamber the animals were either confined in a cage or tied, so that while they had a certain amount of freedom they could not come in contact with the stove or otherwise injure themselves or the apparatus. At the lower temperatures they usually rested quietly or slept unless disturbed for purposes of observation. At 45° and 50°C. they were somewhat restive during the first few minutes of the exposure but later became quiet.

All of the blood samples were drawn from the jugular vein by venepuncture, in no case was venesection practiced.

For the convenience of the reader the results are presented in the form of graphs. These have been plotted from the means calculated from the various values obtained at the end of each interval and at each temperature. In order to obtain some idea of the mean average condition of the animals at the beginning of the experiments, the means and the mean standard deviations for all of the initial values of the several determinations were calculated. These mean initial

values we have used as a base with which to compare the effects of the experimental procedures. This was done by adding algebraically to each of the means of an experimental series an amount sufficient to make the initial value of that series equal to the mean of all the corresponding initial determinations. Exactly what was done will be made clear by reference to table 1. In this table are shown the means obtained for the initial determinations and those for a single

TABLE 1

To illustrate the method used in tabulation and the derivation of the data used in plotting the curves

	BODY WEIGHT	RECTAL TEMPERATURE	PER 100 CC. OF BLOOD					
			CO_2 content	CO_2 capacity	O_2 content	O_2 capacity	Glucose	Total solids
Initial values, 47 observations								
	Kg	*°C.*	*cc.*	*cc.*	*cc.*	*cc.*	*mgm.*	*mgm.*
Mean values		38.7	46.7	62.5	17.7	25.1	91	21.7
Mean standard deviation			±4.8	±4.9	±3.4	±3.1	±11	±2.1
Chamber temperature 20°C. Relative humidity 0.46; 12 observations								
Initial mean	14.8	38.9	45.2	67.0	18.4	25.3	92	22.2
Correction added		−0.2	1.5	−4.5	−0.7	−0.2	−1	−0.5
Modified mean		38.7	46.7	62.5	17.7	25.1	91	21.7
Mean standard deviation			±5.4	±3.3	±3.0	±3.5	±12	±2.0
2nd hour, mean	14.8	39.0	45.8	66.9	19.0	25.7	87	22.4
Modified mean		38.6	47.3	62.4	18.3	25.5	86	21.9
Mean standard deviation			±5.6	±3.3	±3.0	±3.9	±17	±1.8
4th hour, mean	14.7	38.2	46.0	67.7	18.8	25.6	85	22.8
Modified mean		38.0	47.5	63.1	18.1	25.4	84	22.3
Mean standard deviation			±5.3	±3.7	±3.1	±3.0	±16	±2.5
6th hour, mean	14.7	38.3	46.0	67.9	18.8	25.5	83	22.3
Modified mean		38.1	47.5	63.4	18.1	25.3	82	21.8
Mean standard deviation			±5.2	±3.6	±3.4	±3.4	±15	±1.9

temperature—20°. Together with the means are shown the correction which was added and the modified mean so obtained. This last was used in all cases in plotting the curves shown. (cf. Scott and Ford (9).)

The formula used in calculating the mean standard deviation was:

$$\sigma = \frac{\sqrt{\dfrac{\Sigma (d)^2}{N - 1}}}{\sqrt{N}}$$

where σ = the mean standard deviation; d = the arithmetical difference between the individual determinations and the mean for the series, and N the number of observation.

It is planned to publish shortly the complete data obtained in this research together with additional material as a bulletin of the United States Public Health Service. It is hoped that those interested in the detailed results will make use of this publication.

TABLE 2

To show the number of observations made and the individual dogs used in the first series, embracing determinations of oxygen content and capacity, carbon dioxide content and capacity, blood sugar and total solids

CONDITIONS		OBSERVATIONS ON DOG						TOTAL OBSERVATIONS
Temperature	Mean relative humidity	E	H	J	M	P	Q	
°C.								
Initial		7	4	5	10	10	10	46
20	46	2	2	2	2	2	2	12
30	43	2	2	2	2	2	2	12
40	39	2	0	1	2	2	2	9
45	35	1	0	0	2	2	2	7
50	28	0	0	0	2	2	2	6

TABLE 3

To show the number of observations made and the individual dogs used in the second series, embracing determinations of the concentration of hydrogen ion and carbon dioxide content of the oxalated plasma

TEMPERATURE	OBSERVATIONS ON DOG				TOTAL OBSERVATIONS
	M	P	S	T	
°C.					
20	1	1	1	1	4
30	1	1	1	1	4
40	1	1	1	1	4
45	2	2	2	2	8
50	2	2	2	2	8

Experimental results and discussion. The total number of experiments which were carried out together with the experimental conditions to which the animals were subjected as well as the individual dogs which served as subjects are indicated in tables 2 and 3.

I. *The effects of various environmental temperatures upon the body temperature.* The changes in the body temperature during exposure to the several conditions studied are shown graphically in figure 1.

The mean body temperature for forty-seven initial observations was 38.7°C. It was found that the body temperature fell slightly for a time and then remained at a fairly constant level for the remainder of the period of observation. This agrees with the results reported by the New York State Commission of Ventilation for men when they were subjected to similar conditions (10).

At environmental temperatures of 30° the history for the dogs was much the same as for 20° except that the fall in body temperature was not quite so marked. The New York State Commission

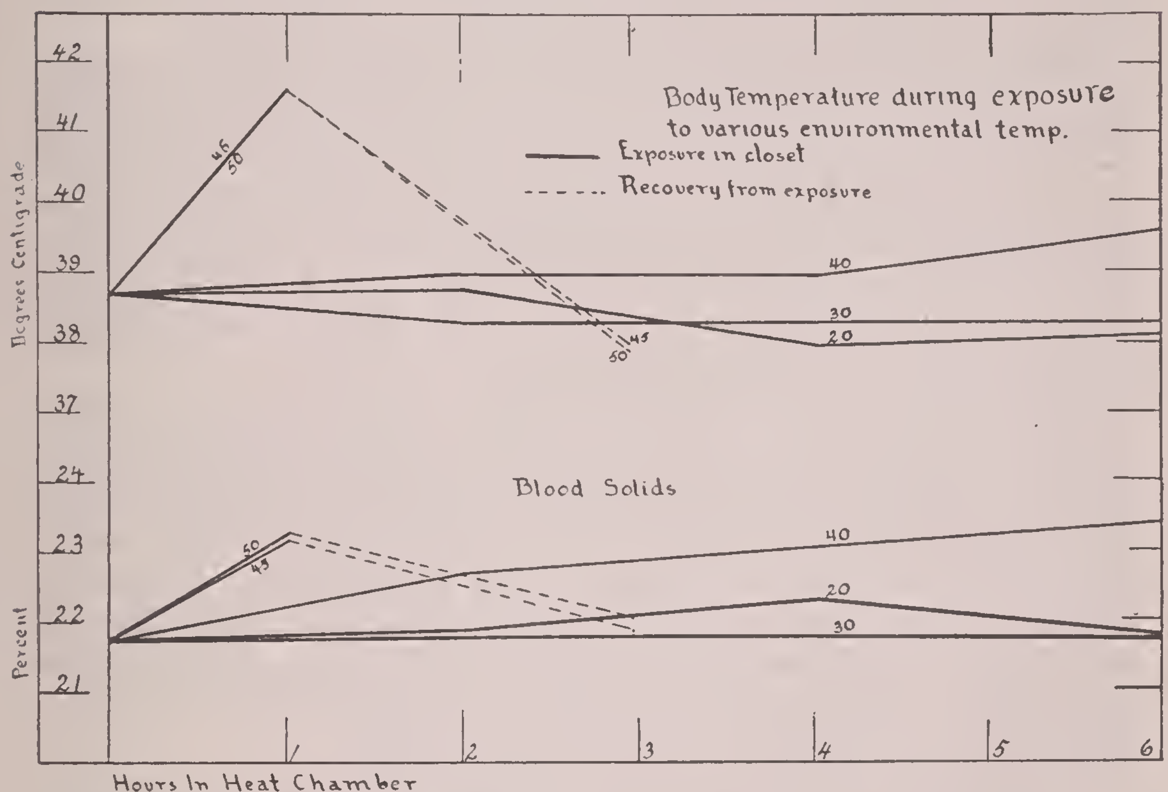

Fig. 1. Curves to show the relation between various environmental temperatures and the temperature of the body and the total solids of the blood of dogs.

of Ventilation reported a slight rise of body temperature in men when they were exposed to an environmental temperature of 30°, though in their case the humidity was 80 per cent, much higher than in any of our experiments. The explanation of this behavior is not clear to us although it may possibly be related to the normal diurnal variations in the body temperature as our observations and those of the Commission were begun in the morning and continued for some time through the day. Or again it may be related to the decreased muscular activity which accompanies confinement in the chamber and to the fact that no food was taken during the course of the observations. This latter interpretation seems the more probable

in view of the fact that the diurnal curves usually shown are highest in the late afternoon and hence vary in the sense opposite to that observed by us.

A consideration of the work of Rubner (11) is of interest at this point, for he has shown that at 20°C. the dog manifests no increase in the rate of metabolism, and that this condition of unchanging metabolism persists while the environmental temperature is raised to at least 30°. He has further demonstrated that in the fasting animal the minimum energy release occurs at temperatures of from 30° to 35°C. This might be called the basal energy requirement, or the minimum energy release compatible with mammalian life.

When the temperature of the chamber is raised to 40°, the response is quite different. Here we find a *rise* of 1 degree in body temperature during the six-hour period of observation, and as a rise was apparent at the end of the first hour of exposure there was no evidence of an initial fall as observed in the two previous cases. The temperature remains constant during the middle period, the rise being confined to the first and last two-hour periods. Whether or not this is of significance we are not prepared to say.

At temperatures of 45° and 50° a very marked rise of the rectal temperature was noted, which apparently began at once. In fact this rise was so sharp that at the end of one hour the body temperature had risen to such a point that it was not deemed safe to continue the experiments at these temperatures for a longer time. On removal of the animal from the chamber the body temperature rapidly fell and two hours after removal the body temperature was subnormal, or about 36°. This subnormal temperature reminds one of the conditions in certain stages of heat stroke in man.

It will be noted that the body temperature is the same whether the animal had been exposed to an environmental temperature of 45° or 50°. This remarkable fact of a similar physiological response to conditions of different severity was noted in some of the other factors studied it being especially marked for those having to do with the carbon dioxide. The organism seems to yield with increasing rapidity as the strain impressed upon it becomes more severe, until a certain limit is reached at which point great resistance is interposed by the organism against any further change. If the strain is increased so that the organism is pushed beyond this point, it will recover with great difficulty, if at all, unless external aid is given. This same type of physiological limitation was noticed by Henderson and Haggard (12) during their work on low levels of carbon dioxide and alkali reserve induced by ether. It was also noticed by Britton in his studies on cooling. In order to lower the temperature of his

animals below what might be called the critical point he found it necessary to subject them to anesthesia until it had been passed, after which the anesthesia was no longer necessary and the body temperature continued to fall so long as the animal was exposed to an environmental temperature lower than the body temperature.

II. *The effects of various environmental temperatures upon the oxygen content and upon the amount of hemoglobin in the blood.* Considering first the oxygen capacity (hemoglobin) we find very little variation throughout the series. In fact, all of the mean values are within the limits of the mean standard deviations of the 20° series and so from a purely statistical standpoint are without significance. The direction of the slight variations which do occur fits so nicely with other circumstances, however, that one hesitates to dismiss them without further discussion. (Fig. 2.)

The changes noted at 20° and 30°, if not entirely fortuitous, may be an example of the diurnal changes studied for man and the goat by Dreyer, Bazett and Pierce (14). At temperatures of 40° and above there is a slight tendency for the oxygen capacity to increase, this tendency becoming somewhat more marked as the environmental temperature rises. This increase is paralleled by an increase in the total solids, and we have related it simply to an increase in the concentration of the blood due to the excessive evaporation of water, accompanied by an inability of the water reservoirs to supply water at a rate sufficient to meet the demand made upon them at these high temperatures.

The fact that there was no increase in the oxygen capacity during the first two-hour period of exposure to a temperature of 40° would seem to bear out this interpretation. It might fairly be assumed that at this temperature the loss would not be so rapid but that sufficient time would be permitted for equilibration and that there had not yet occurred so great a loss that the available store of water had become seriously depleted. The later rise, then, was probably due to an actual depletion of the available water below a limit where the original concentration of the blood could be maintained.

At 45° and 50° it may be presumed that while the actual quantity of water which has been lost from the tissues during the first hour of exposure is not of itself serious, the rate of loss of water from the blood is so rapid that the organism is unable to maintain the original concentration of the blood. This interpretation is further supported by the rapid return of the oxygen capacity and of the total solids to their original level during the first two hours after the animal was removed from the chamber.

A very slight fall is noted in the oxygen capacity of the animals exposed to 30°. A comparison of this fall with the mean standard deviation of the 20° series, however, indicates that it is too small to be of significance from the standpoint of statistics. Some biological considerations, on the contrary, seem to show that it may have some importance; but this evidence is not sufficient to warrant discussion at the present time.

There is a fairly marked fall in the oxygen content of the venous blood of animals exposed to a temperature of 30° as compared with

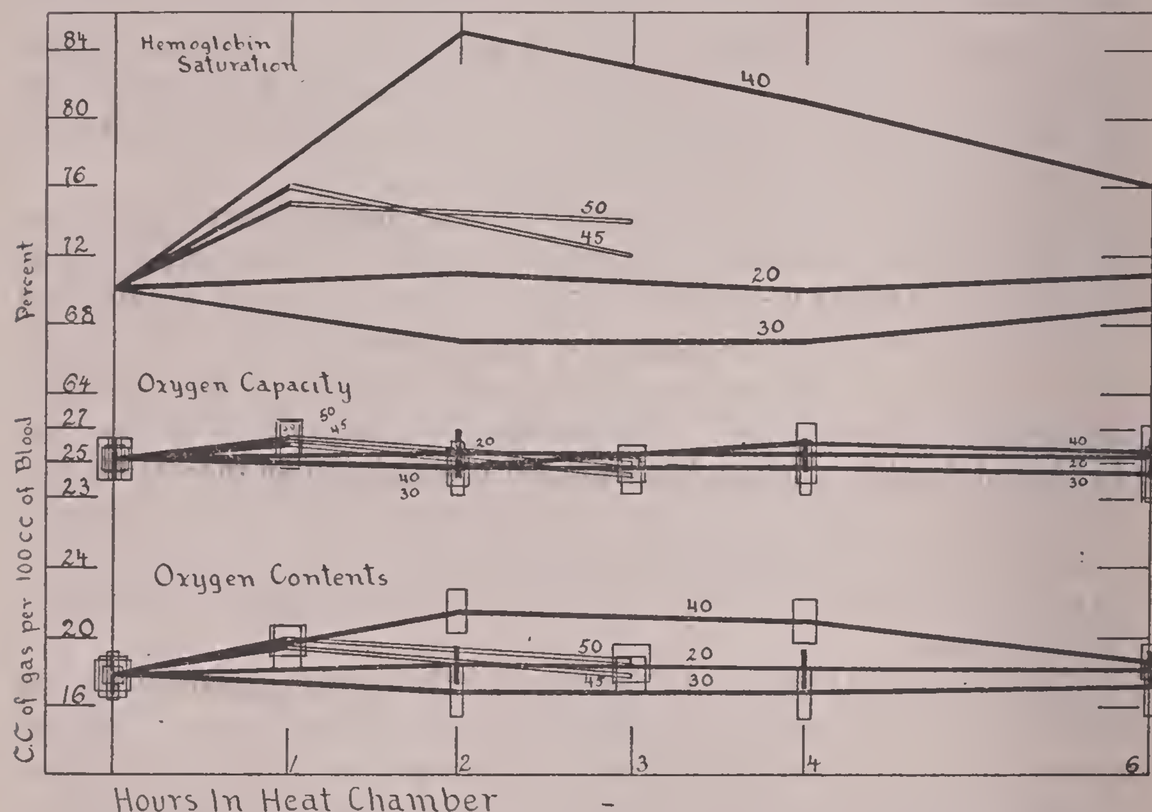

Fig. 2. Curves to show the effects of various environmental temperatures upon the oxygen capacity, oxygen content and the percentage of oxygen saturation of the venous blood of dogs.

that of animals exposed to a temperature of 20°. This drop we believe to be a reflection of the manner in which the animals respond to the two temperatures. At 30° and the humidities at which we were working, there seems to be nearly an equilibrium between the heat generated in the basal metabolism and the heat lost to the environment. (Cf. Voit (15).) The animals are quick to take advantage of this and stretch themselves out and take life easily. Hyperpnea has not yet become necessary to keep the temperature of the body down. All muscular movements, and consequently heat generation, are at a minimum. The net result is a considerably

reduced aeration of the blood, as well as a reduced circulation and consequently a reduced oxygen content, especially of the venous blood.

At 40° there is a considerable increase in the rate of respiration, and correlated with this, a rather marked increase in the oxygen content of the blood. The rate of increase in the oxygen content is slightly greater at 45° and 50°, respectively, than it is at 40°, but the increased rates are not nearly so great as might be expected when one compares them with that occurring between 30° and 40°. There are at least two factors concerned in this: First, while the rate of respiration continues to increase as the environmental temperature continues to rise it becomes progressively shallower (fig. 3), so that while the efficiency of the respiratory apparatus as a cooling mechanism may rise because of the increased passage of air over the membranes of the mouth and throat and a consequent increase in the vaporization of water, its efficiency as a means of aerating the blood does not increase in anything like the same ratio, if at all. Second, with the increased body temperature which accompanies exposure to these high environmental temperatures the rate of metabolism is increased and this would of course be reflected in a decreased oxygen content of the venous blood provided that there was not at the same time a considerable increase in the amount of oxygen carried in the arterial blood, which from the evidence just discussed, is probably not the case. The curves showing the percentage of saturation (fig. 2) are very satisfactorily explained on this hypothesis.

III. *The effects of various environmental temperatures upon the carbon dioxide content and upon the alkali reserve of the blood.* There is no change in the carbon dioxide capacity of the blood during an exposure of six hours to a temperature of 20° or of 30°, as is shown in figure 4, where it will be seen that the two curves are identical within the limits of the mean standard deviation and that both are horizontal.

When the environmental temperature is raised to 40° there is a fairly rapid fall during the first four hours and a somewhat slower fall during the remaining two hours. At 45° and 50° there is a very rapid depletion of the alkali reserve as shown by the carbon dioxide capacity, this depletion being almost identical in degree for the two temperatures. This is a very good illustration of the critical point previously mentioned in the discussion of body temperature. We believe that the changes noted result directly from the equilibration necessitated by the washing out of the carbon dioxide which, in turn, is caused by the hyperpnea due to the high temperatures—a hyperpnea which may even become dyspnea if the exposure is long continued.

The carbon dioxide content (fig. 5) gives a similar picture, except that here a slight rise is noted in the animals exposed to an environmental temperature of 30°. This probably results from the same cause as the corresponding slight depression of the oxygen content

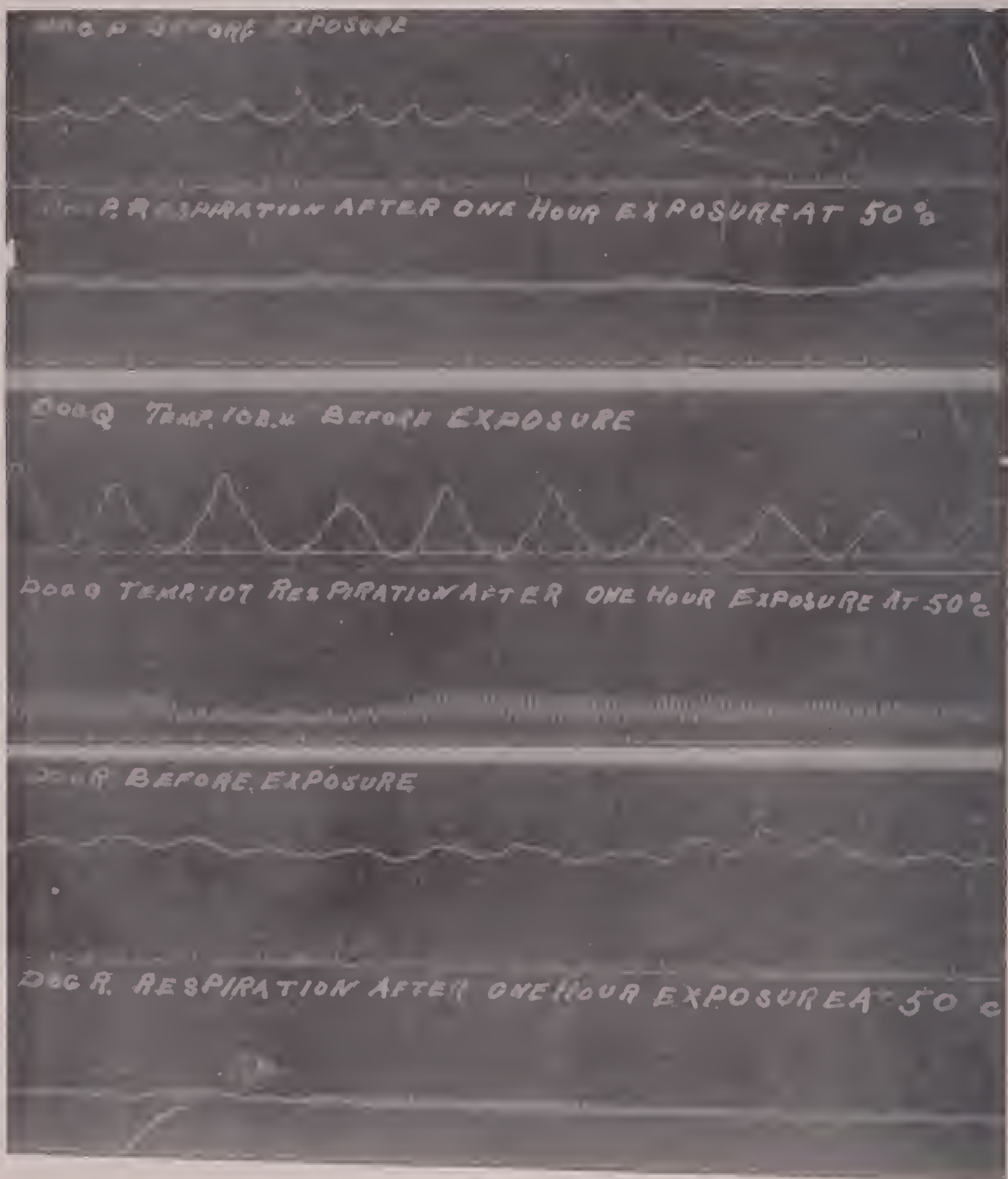

Fig. 3. Pneumographic tracings to show the relative rate and depth of respiration of dogs subjected to environmental temperatures of 20° and 50°C.

which was noted for the same condition, i.e., a small decrease in the rate of metabolism, which would be, under these conditions, at its lowest ebb as shown by Rubner and others. This decreased metab-

olism would result in a slight lowering of the rates of respiration and circulation.

IV. *The effects of various environmental temperatures upon the hydrogen-ion content of the plasma.* The hydrogen-ion concentration

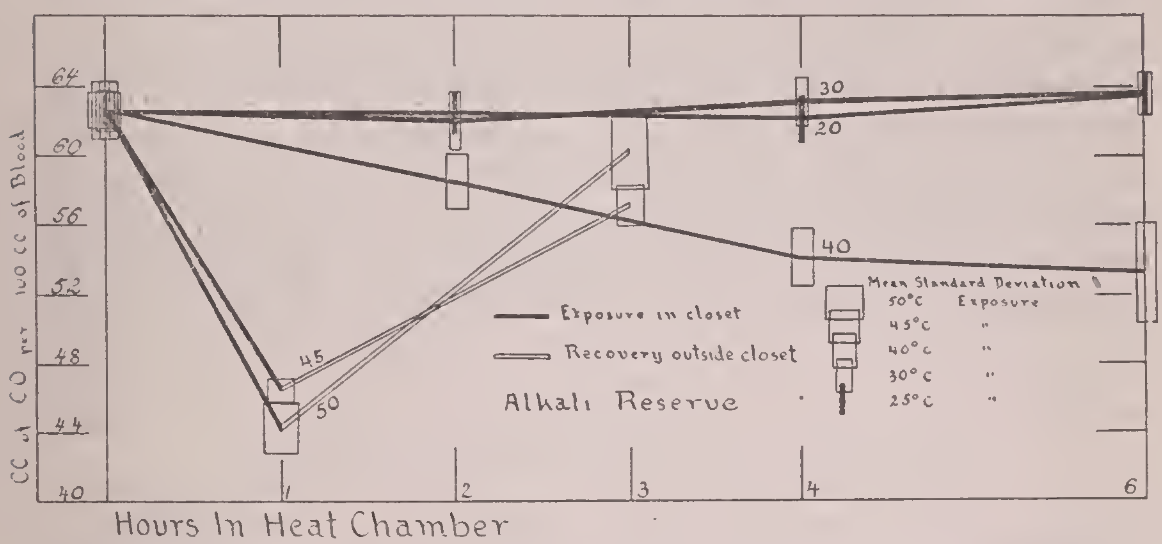

Fig. 4. Curves to show the effects of various environmental temperatures upon the alkali reserve of the blood of dogs as determined by the carbon dioxide capacity.

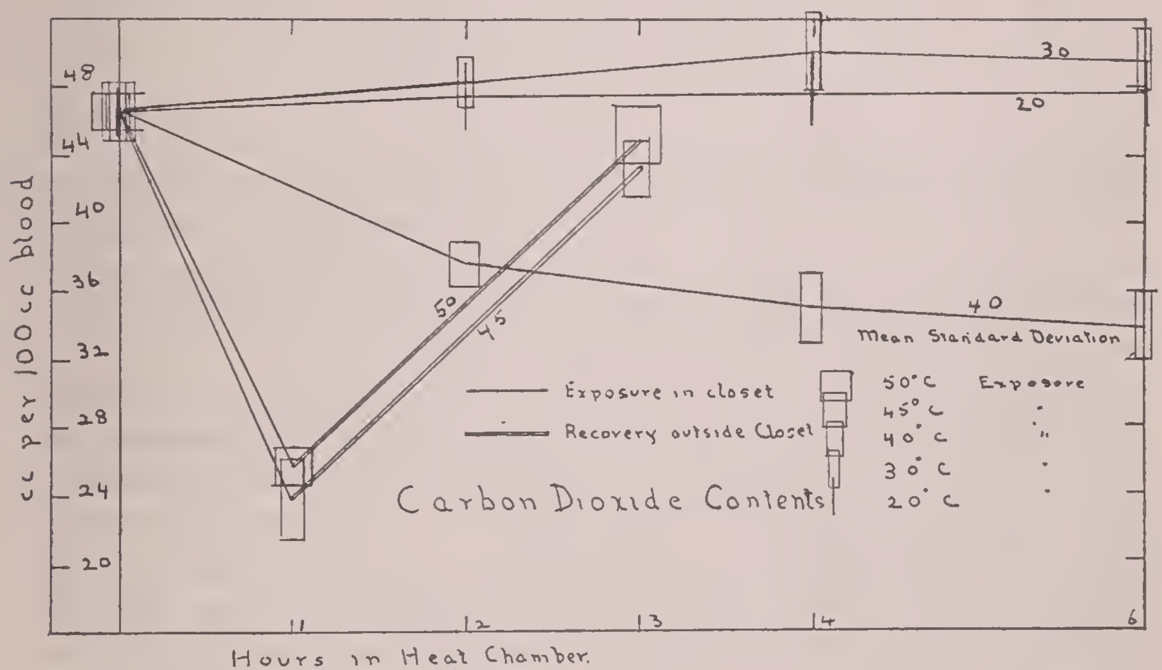

Fig. 5. Curves to show the effects of various environmental temperatures upon the carbon dioxide content of the venous blood of dogs.

expressed as pH remains constant for at least six hours when the animals are exposed to temperatures of 20° or 30° (table 4) and falls within the normal acid-base balance, or area 5 of the Van Slyke

chart (16). At 40° with an increased rate of respiration and the resultant fall in the carbon dioxide content and the alkali reserve, we find that the blood index has passed from area 5 to area 6 of the Van Slyke chart, or into the region of compensated carbon dioxide deficit. The alkali reserve likewise falls thus preventing an abnormal alkalinity. As the strain becomes greater with environmental temperatures of 45° and 50°, the pH increases from the normal of 7.55 to 7.79 and to 7.84 for the two temperatures respectively. The carbon dioxide of the plasma has dropped to 29.9 and to 26.3 volumes per cent and the plasma index has passed into area 2 or 3 of the Van Slyke chart or into the region of uncompensated carbon dioxide deficit as the result of an excessive loss of carbon dioxide. This loss of carbon

TABLE 4

To show the effect of various environmental temperatures upon the concentration of the hydrogen ion and carbon dioxide content of the plasma

TEMPERATURE OF CHAMBER	BEFORE EXPOSURES		AFTER ONE HOUR EXPOSURE		AFTER SIX HOURS EXPOSURE	
	pH	CO_2 content	pH	CO_2 content	pH	CO_2 content
°C.						
20	7.57	52.4	7.57	52.4	7.57	55.4
40	7.57	52.4	7.56	46.6	7.56	39.5
45	7.57	52.4	7.79	29.89		
50	7.57	52.4	7.83	26.3		

dioxide was induced by an increase of the respiratory rate which was evidently brought about by some stimulus other than an increased concentration of the hydrogen-ion. The same condition, also accompanied by hyperpnea, has been observed by Bazett and Haldane (17) in man when immersed in warm baths.

Kahn (18) and Barbour (19) are of the opinion that the mechanism causing the increased rate of respiration is the increased temperature of the blood, that is, it is the direct result of the increased body temperature. It is known that cellular activities in general increase, within limits, with the temperature and there is no apparent reason for excepting the respiratory center from this category. It was at first thought that the stimulus might be due to a local accumulation of hydrogen-ion within the cells of the respiratory center itself, which might occur as a part of a general tissue anoxemia depending upon the increased stability of the oxyhemoglobin at low carbon dioxide concentrations. (Cf. Bohr (20).) If such an anoxemia should in truth exist one would expect to find it indicated by an accumulation of lactic acid in the blood, but a careful search has failed to show the slightest increase

of this acid in the blood of animals exposed to high temperatures, over the amount occurring under ordinary conditions. It is difficult for us to imagine a significant acidosis occurring in the tissues without its being mirrored in the blood stream.

Our work does not permit us to accept the suggestion of Hill and Flack (21) and of Mayer (22) that fatal termination from over-heating is due to an accumulation of acid. We found a decreased rather than an increased hydrogen-ion concentration in the plasma of all of our animals which recovered from exposure to severe conditions and in none did we find any indication of increased lactic acid. From two animals, Q and R, which died shortly after removal from the chamber after having been exposed to rather severe conditions, blood was drawn only a few minutes before death. The mean values obtained were:

Oxygen content	5.9	Carbon dioxide content	30.5
Oxygen capacity	23.6	Carbon dioxide capacity	36.7

Hydrogen-ion determinations were not made, but from the Henderson nomogram (23) the pH may be presumed to have been about 7.4, which would not indicate acidosis. (Compare Henderson (24).)

Since the respiratory efforts gave every indication of the passage of at least a normal volume of air up to the time that the samples were taken we have interpreted the changes which occurred as indicating circulatory rather than respiratory failure, this having been induced by the overload thrown on the circulatory mechanism in the effort to keep the body temperature down.

V. *The relation between the concentration of the sugar in the blood and the temperature of the environment.* The changes in the concentration of the sugar in the blood (fig. 6) are rather hard to explain in a manner which is consistent for all of the conditions studied. At 20° there is a fairly uniform fall throughout the six-hour period of observation. This is in entire agreement with the observation of Scott and Hastings (25) and can hardly be related to the ingestion of food since sufficient time was allowed for this factor to become constant before the first sample was drawn. The only explanation which occurs to us is that the animals were becoming progressively quieter as the experiments proceeded and consequently were mobilizing less and less sugar. Whether such a decrease in the rate of mobilization of sugar is the direct result of lessened excitement, or whether it is due to the operation of an unknown factor which tends to equilibrate the concentration of sugar in the blood with the metabolic requirements of the organism for sugar, is a matter which we are unable to discuss at present. Aside from this factor which may be assumed, for the time being, to have been constant

throughout the research, it is to be noted that when the corresponding periods of the different series are compared a rough agreement between the concentration of the sugar in the blood and the body temperature is noted. The 45° series forms an exception to the rule, however, for at this environmental temperature the body temperature is almost identical with that which occurs when the animals are exposed to a temperature of 50°; while the concentration of sugar occupies a position midway between that found at 40° and that at 50°. This rise in the blood sugar is then not exclusively dependent upon the body temperature but seems also to be associated with the environmental temperature

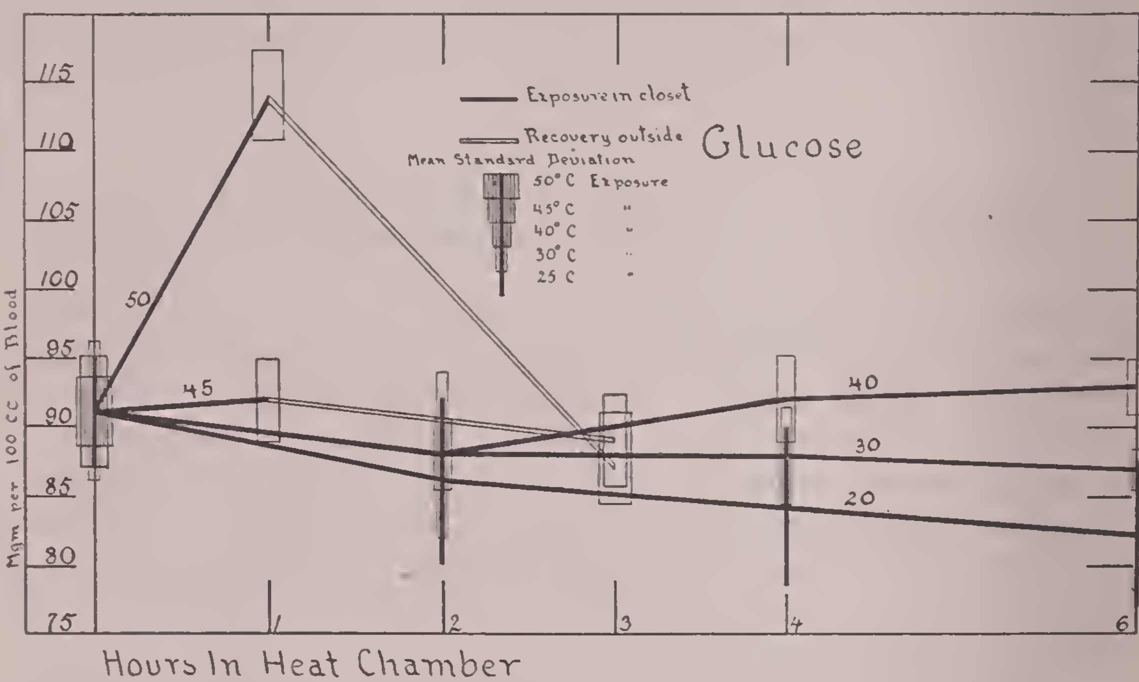

Fig. 6. Curves to show the effects of various environmental temperatures upon the concentration of glucose in the venous blood of dogs.

in a more direct manner. It is apparently not dependent upon any emotional disturbances resulting from the exposure to the higher temperatures. We hope to be able to give further evidence regarding this phase in a later paper. Lépine (26) attributes the hyperglycemia which is occasionally present in fever to an irritation of the fourth ventricle by the fever toxins. The increase in the concentration of sugar which Freund and Marchand (27) report in fever is only of such a degree that it may be accounted for by changes in the concentration of the blood. We are not, however, able to explain our results in this manner since we found the increase in the sugar to exceed that of the total solids; in one case there was an increase in the sugar of 100 per cent while at the same time the total solids increased only 25 per cent.

VI. *The relation between the total solids of the blood and the environmental temperature.* The total solids of the blood tend to increase as the environmental temperature rises and we have been unable to observe the dilution mentioned by Barbour (28) in the report of his experiments with hot and cold baths. Our results seem to be more in line with the results which he obtained in coli fever (29). There is no doubt some mechanism by which the total blood volume is regulated, and our results should be considered as indicating some interference with the activity of this mechanism. At high temperatures the rate of replacement of water cannot keep pace with the rate of its loss and a certain amount of concentration results. There is, however, a fairly large factor of safety for it is not until the concentration of the blood approaches 25 per cent that pathological symptoms occur from this cause.

SUMMARY

1. During an exposure of six hours to an environmental temperature of 20° or of 30° there was a drop in body temperature, probably due to a decrease of muscular activity. At 40° there was an increase of 1 degree in body temperature without an initial drop. At 45° and 50° the body temperature rose within an hour to such a height that it was deemed unsafe to continue the experiments at these temperatures for a longer time.

2. The oxygen capacity of the blood showed no change during an exposure to the different temperatures that cannot be accounted for by the diurnal changes in the hemoglobin or by the concentration of the blood due to the excessive evaporation of water.

3. The oxygen content of the blood remains unchanged at 20°, but shows a drop at 30° which is probably associated with the low rate of metabolism at this temperature. At 45° and 50° there is a slight increase in the oxygen content due to the increased aeration of the blood at these temperatures, but this increase is not in direct proportion to the increased passage of air over the membranes of the mouth and throat.

4. At temperatures of 20° and 30° the carbon dioxide capacity of the blood remains unchanged, while at 40° there is a sharp fall during the first four hours followed by a slower fall during the next two hours. At temperatures of 45° and 50° there is a rapid depletion of the carbon dioxide capacity from the beginning, which is almost identical for these two temperatures.

5. The carbon dioxide content follows the capacity except that at 30° there is a slight rise for the same reason that the oxygen content falls.

6. The hydrogen-ion content of the plasma remains unchanged during an exposure of the animal to temperatures of 20°, 30° and 40° for six hours, but decreases at temperatures of 45° and 50° due to the excessive pulmonary ventilation at these temperatures with the consequent washing out of the carbon dioxide and without a compensatory loss of alkali from the blood.

7. The concentration of blood sugar falls during an exposure to temperatures of 20° and 30°. This fall is probably associated with inactivity of the animal during the course of the experiment. At 40° it falls during the first two hours, to increase during the following four hours. At 45° no change was noted during an hour's exposure while at 50° there was a sharp rise during this time.

8. The blood solids at 20° and 30° showed only the usual diurnal changes, while at 40°, 45° and 50° the concentration of the blood increased with the environmental temperature, no initial drop having been observed.

BIBLIOGRAPHY

(1) Van Slyke: Journ. Biol. Chem., 1917, xxx, 347.
(2) Van Slyke and Stadie: Journ. Biol. Chem., 1921, xlix, 1.
(3) MacLean: Biochem. Journ., 1919, xiii, 135.
(4) Hastings and Hopping: Proc. Soc. Exper. Biol. and Med., 1923, xx, 254.
(5) Brown: Journ. Amer. Chem. Soc., 1922, xliv, 423.
(6) Scott and Flinn: Journ. Biol. Chem., 1923, l, Proc. Soc., 32.
(7) Cullen: Journ. Biol. Chem., 1922, lii, 501.
(8) Hastings: Jour. Ind. Eng. Chem., 1921, xiii, 1056.
(9) Scott and Ford: This Journal, 1923, lxiii, 520.
(10) Ventilation Report of the New York State commission of Ventilation; 1923, p. 51 et seq.
(11) Rubner: Energiegesetz. 1902, pp. 105–137.
(12) Henderson and Haggard: Journ. Biol. Chem., 1918, xxxiii, 333.
(13) Britton: Quart. Journ. Exper. Physiol., 1922, xiii, 55.
(14) Dreyer, Bazett and Pierce: Lancet, 1920, ii, 588.
(15) Voit: Zeitschr. f. Biol., 1901, xli, 125.
(16) Van Slyke: Journ. Biol. Chem., 1921, xlviii, 153.
(17) Bazett and Haldane: Journ. Physiol., 1921, lv, 125.
(18) Kahn: Arch. f. Physiol., Supple. 1904, 31.
(19) Barbour: Physiol. Rev., 1921, i, 295.
(20) Bohr, Hasselbach and Krogh: Skand. Arch. Physiol., 1907, xvi, 390.
(21) Hill and Flack: Journ. Physiol., 1909, xxxviii, Proc. lvii and lxi.
(22) Mayer: Carnegie Pub. no. 252.
(23) Henderson: Journ. Biol. Chem., 1921, xlvi, 411.
(24) Henderson: This Journal 1910, xxv, 397.
(25) Scott and Hastings: Proc. Soc. Exper. Biol. and Med., 1920, xvii, 120.
(26) Lepine: Rev. Med., 1915, xxxiv, 657.
(27) Freund and Marchand: Arch. f. Exper. Path. u. Physiol., 1913, lxxiii, 276.
(28) Barbour: Proc. Soc. Exper. Biol. and Med., 1921, xviii, 184.
(29) Barbour and Howard: Proc. Soc. Exper. Biol. and Med., 1920, xvii, 148.

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Lactic Determination, Scott and Flinn, Journ. Biol. Chem., 1922, 1 proc. Soc. 32.

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